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I: Multiple choices. Please choose the best answer for each question. (30%) 1. Which amino acids are products of the shikimate pathway? (a) lysine, serine, arginine (d) phenylalanine, tryptophan, tyrosine (b) methionine, leucine, valine (e) phenylalanine, tyrosine, histidine (c) aspartate, methionine, threonine 2. There are two nitrogen atoms eliminated from the human body in the urea molecule. One of these comes from ammonium ion through carbamoyl phosphate. What compound brings the other nitrogen directly to the urea cycle? (a) Aspartate (b) Asparagine (c) Glutamate (d) Glutamine (e) Methionine 3. The nodules on roots of legumes that are involved in nitrogen fixation are red in color due to the presence of a protein called leghemoglobin. What purpose does this protein serve? (a) It binds oxygen and makes it available to the nitrogenase enzyme complex, which needs oxygen to function properly. (b) It is part of the nitrogenase complex. (c) It binds oxygen to help keep it away from the nitrogenase enzyme complex, which is inhibited by oxygen. (d) It has nothing to do with nitrogen fixation; it serves a different function in legume roots. (e) none of the above. 4. What causes the activity of PEPCK in liver cells to increase in response to glucagon? (a) Binding of the glucagon receptor to the PEPCK gene. (b) Phosphorylation of PEPCK by protein kinase A. (c) Phosphorylation of PEPCK by MAP kinase. (d) Phosphorylation of CREB by protein kinase A. (e) Phosphorylation of STAT by JAK kinase. 5. Exercise helps control the symptoms and consequences of Type II diabetes because its effect on muscle is to stimulate the uptake of (b) ketone bodies. (c) lactic acid. (d) VLDL. (a) glucose. (e) calcium. 6. Non-steroidal anti-inflammatory drugs (NSAIDS) like aspirin and ibuprofen act by blocking production of: (a) biological waxes. (b) prostaglandins. (c) sphingolipids. (d) vitamin D. (e) none of the above. 7. Multivalent scaffold proteins and membrane rafts in signaling the specificity of signaling pathways includes all of the following except: (a) Flippase-catalyzed movement of phospholipids from the inner to the outer leaflet. (b) migration of signal proteins into membrane rafts. (c) Phosphorylation of target proteins at Ser, Thr, or Tyr residues.

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(d) The ability to be switched off instantly by hydrolysis of a single phosphate-ester bond.(e) the assembly of large multiprotein complexes.8. Chylomicrons carry in the?

(a) Triacylglycerols; cell (d) Fatty acids; blood

- (b) Triacylglycerols; blood (e) Fatty acids; cell
- (c) Cholesterols; blood

9. The normal sequence of action of these components of the hormonal hierarchy is:

- (a) adrenal cortex \rightarrow hypothalamus \rightarrow anterior pituitary
- (b) anterior pituitary \rightarrow adrenal cortex \rightarrow hypothalamus
- (c) anterior pituitary \rightarrow hypothalamus \rightarrow adrenal cortex
- (d) hypothalamus \rightarrow adrenal cortex \rightarrow anterior pituitary
- (e) hypothalamus \rightarrow anterior pituitary \rightarrow adrenal cortex
- 10. Glutamine is a nitrogen donor in the synthesis of:
 - (a) CTP. (b) dTTP. (c) inosinic acid (IMP). (d) orotate. (e) UMP.
- 11. In comparing fatty acid biosynthesis with β -oxidation of fatty acids, which of the following statements is *incorrect*?
 - (a) A thioester derivative of crotonic acid (*trans*-2-butenoic acid) is an intermediate in the synthetic path, but not in the degradative path.
 - (b) A thioester derivative of D- β -hydroxybutyrate is an intermediate in the synthetic path, but not in the degradative path.
 - (c) Fatty acid biosynthesis uses NADPH exclusively, whereas β -oxidation uses NAD⁺ exclusively.
 - (d) Fatty acid degradation is catalyzed by cytosolic enzymes, fatty acid synthesis by mitochondrial enzymes.
 - (e) The condensation of two moles of acetyl-CoA in the presence of a crude extract is more rapid in bicarbonate buffer than in phosphate buffer at the same pH; the cleavage of acetoacetyl-CoA proceeds equally well in either buffer.
- 12. Which of these statements about the regulation of cholesterol synthesis is not true?
 - (a) Cholesterol acquired in the diet has essentially no effect on the synthesis of cholesterol in the liver.
 - (b) Failure to regulate cholesterol synthesis predisposes humans to atherosclerosis.
 - (c) High intracellular cholesterol stimulates formation of cholesterol esters.
 - (d) Insulin stimulates HMG-CoA reductase.
 - (e) Some metabolite or derivative of cholesterol inhibits HMG-CoA reductase.
- 13. When blood glucose is abnormally low, the pancreas releases:
 - (a) epinephrine. (b) glucagon. (c) glucose. (d) insulin. (e) trypsin.
- 14. If glucose labeled with ¹⁴C at C-1 were the starting material for amino acid biosynthesis, the product(s)

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that would be readily formed is (are):

- (a) serine labeled at the carboxyl carbon.
- (b) serine labeled at alpha carbon.
- (c) serine labeled at the R-group carbon.

15. The synthesis of purine and pyrimidine nucleotides differ in that:

- (a) ATP is required in the synthesis of purines but not in the synthesis of pyrimidines.
- (b) purine biosynthesis starts with the formation of PRPP, whereas pyrimidines incorporate the PRPP near the end of the pathway.

(d) all of the above.

(e) none of the above.

- (c) purine formation requires a THF derivative, whereas pyrimidine formation does not.
- (d) pyrimidine biosynthesis is tightly regulated in the cell, whereas purine biosynthesis is not.
- (e) pyrimidines go through many steps, adding a single carbon or nitrogen each time, whereas the basic skeleton for purines is formed by two main precursors.

II (30%)

有一篇標題為 Intracellular metabolite profiling of *Fusarium oxysporum* converting glucose to ethanol 的研究論文,其摘要如下:

The filamentous fungus *Fusarium oxysporum* is known for its ability to produce ethanol by simultaneous saccharification and fermentation (SSF) of cellulose. However, the conversion rate is low and significant amounts of acetic acid are produced as a byproduct. In this study, the growth characteristics of *F. oxysporum* were evaluated in a minimal medium using glucose as the sole carbon source in aerobic, anaerobic and oxygen-limited batch cultivations. Under aerobic conditions the maximum specific growth rate was found to be 0.043 h^{-1} , and the highest ethanol yield (1.66 mol/mol) was found under anaerobic conditions. During the different phases of the cultivations, the intracellular profiles were determined under aerobic and anaerobic conditions. The profiles of the phosphorylated intermediates indicated that there was a high glycolytic flux at anaerobic growth conditions, characterized by high efflux of glyceraldehyde-3-phosphate (G3P) and fructose-6-phosphate (F6P) from the pentose phosphate pathway (PPP) to the Embden–Meyerhof–Parnas (EMP) pathway, resulting in the highest ethanol production under these conditions. The amino acid profile clearly suggests that the TCA cycle was primarily active under aerobic cultivation. On the other hand, the presence of high levels of γ -amino-n-butyric acid (GABA) under anaerobic conditions suggests a functional GABA bypass and a possible block in the TCA cycle at these conditions.

依照摘要的敘述,回答第1-5題 (每題答對得3%,答錯倒扣1%): 1. Fusarium oxysporum 是一種(A)病毒 (B)細菌 (C)真菌 (D)植物 (E)原生生物

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2.分析 F. oxysporum 細胞的 profiles of phosphorylated intermediates 可以得知下列哪一個代謝途徑的 流量 I. PPP 途徑 II. EMP 途徑 III. TCA cycle IV. GABA bypass (A)只有 I (B)只有 III (C)只有 I 和 II (D)只有 III 和 IV (E)只有 I, II 和 III 3.在最佳條件下,利用 100g 葡萄糖作為唯一碳源, F. oxysporum 可產生的酒精量最接近 (A) 1.7 g (B) 17 g (C) 40 g (D) 60 g (E) 80 g 4. 無氧的培養條件使 Fusarium oxysporum 細胞內的哪一個代謝途徑中斷? I. PPP 途徑 II. EMP 途徑 III. TCA cycle IV. GABA bypass

(A)只有 I (B)只有 III (C)只有 I 和 II (D)只有 III 和 IV (E)只有 I, II 和 III

5. Fusarium oxysporum 利用纖維素為原料發酵產生酒精時,同時產生大量的 (A)乙醛 (B)乙酸 (C) 丙酮 (D)丙酸 (E)丙酮酸

一篇標題為 Feedback-resistant acetohydroxy acid synthase increases valine production in *Corynebacterium glutamicum* 的研究論文,其摘要如下:

Acetohydroxy acid synthase (AHAS), which catalyzes the key reactions in the biosynthesis pathways of branched chain amino acids (valine, isoleucine, and leucine), is regulated by the end products of these pathways. The whole *Corynebacterium glutamicum ilvBNC* operon, coding for acetohydroxy acid synthase (*ilvBN*) and acetohydroxy acid isomeroreductase (*ilvC*), was cloned in the newly constructed *Escherichia coli-C. glutamicum* shuttle vector pECKA (5.4 kb, Km^r). By using site-directed mutagenesis, one to three amino acid alterations (mutations M8, M11, and M13) were introduced into the small (regulatory) AHAS subunit encoded by *ilvN*. The activity of AHAS and its inhibition by valine, isoleucine, and leucine were measured in strains carrying the *ilvBNC* operon with mutations on the plasmid or the *ilvN*M13 mutation within the chromosome. The enzyme containing the M13 mutation was feedback resistant to all three amino acids. Different combinations of branched-chain amino acids did not inhibit wild-type AHAS to a greater extent than was measured in the presence of 5 mM valine alone

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(about 57%). We infer from these results that there is a single binding (allosteric) site for all three amino acids in the enzyme molecule. The strains carrying the *ilvN*M13 mutation in the chromosome produced more value than their wild-type counterparts. The plasmid-free *C. glutamicum* $\Delta ilvA$ $\Delta panB$ *ilvN*M13 strain formed 90 mM value within 48 h of cultivation in minimal medium. The same strain harboring the plasmid pECKA*ilvBNC* produced as much as 130 mM value under the same conditions. 依照摘要的敘述,回答第 6-10 題 (每題答對得 3%,答錯倒扣 1%):

6.野生型棒狀桿菌 Corynebacterium glutamicum 細胞內的 AHAS 酵素活性會受到下列何種氨基酸的 抑制?

- I. alanine
- II. Isoleucine
- III. Leucine
- IV. Valine

(A)只有 I (B)只有 III (C)只有 IV (D)只有 II, III 和 IV (E)I, II, III 和 IV

7.棒狀桿菌Corynebacterium glutamicum AHAS酵素的M13 突變型,其活性<u>不會</u>受到下列何種氨基酸的抑制?

- I. alanine
- II. Isoleucine
- III. Leucine
- IV. Valine

(A)只有 I (B)只有 III (C)只有 IV (D)只有 II, III 和 IV (E)I, II, III 和 IV

8.棒狀桿菌 Corynebacterium glutamicum AHAS 酵素的 M13 突變型,其序列與野生型酵素的序列相比,最可能有幾個氨基酸不同? (A)0 (B)3 (C)8 (D)11 (E)13

9.野生型棒狀桿菌 Corynebacterium glutamicum 細胞內的 AHAS 酵素由幾種不同的次單元構成? (A) 1 (B) 2 (C) 3 (D) 6 (E) 8

10.質體 pECKAilvBNC 在棒狀桿菌 Corynebacterium glutamicum 細胞內可製造出下列何種酵素?

- I. 野生型 acetohydroxy acid synthase
- II. 突變型 acetohydroxy acid synthase
- III. 野生型 acetohydroxy acid isomeroreductase
- IV. 突變型 acetohydroxy acid isomeroreductase

(A)只有 I (B)只有 II (C)只有 I 和 III (D)只有 II 和 III (E)只有 II 和 IV

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III (40%) (from Lehninger)

1.Distinguish between homologs, paralogs, and orthologs as classes of related proteins. (6%)

- 2.Explain what is meant by motifs in protein structure. (5%)
- 3. Why is carbon monoxide (CO) toxic to aerobic organisms? (5%)

4. Give the Michaelis-Menten equation and define each term in it. (8%)

5.Describe one biological advantage of storing glucose units in branched polymers (glycogen, amylopectin) rather than in linear polymers. (5%)

6.Explain how nucleoside triphosphates (such as ATP) act as carriers of chemical energy. (5%)

7. What is the essential difference between a genomic library and a cDNA library? (6%)